Remarks

Applicants have amended the specification to cross reference the parent application which is a PCT application designating the United States. Applicants have also amended the specification to add the required headings and move the text to be in the required order.

Applicants have amended claims 2-7 and 10 to more fully conform with U.S. practice and to delete multiple dependencies. A version of the claims marked up to show the amendments, as well as a clean version of the claims encompassing the amendments, is attached hereto.

Applicants are submitting herewith a copy of the International Search Report which issued on International Application number PCT/NO00/00245, of which the present application is a continuation. All of the publications cited in the International Search Report are listed on the attached Information Disclosure Statement.

Applicants respectfully assert that all amendments are fairly based on the specification, and respectfully request their entry.

Respectfully submitted,

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Claims (marked-up version showing amendments)

[**CLAIMS**]

What is claimed is:

2. (once amended) [A]The method according to claim 1 wherein said vector is selected from peptides, proteins, antibodies, nucleotides, hormones, growth factors, cytokines, carbohydrates, lipids, therapeutic agents and drugs acting through receptor-mediated cell entry.

3. (once amended) [A]The method according to claim 1[or claim 2] wherein the encapsulated microbubbles of step iii) are selected from microbubbles of gas stabilised by a coalescence-resistant surface membrane, a filmogenic protein, a polymer material, a lipid, a non-polymeric and non-polymerisable wall-forming material and a surfactant.

4. (once amended) [A]The method according to claim 3 wherein said surfactant is selected from one or more phospholipids and one or more lipopeptides.

5. (once amended) [A]The method according to [any of claims 1 to 4]claim 1 wherein said gas is a biocompatible gas or gas mixture selected from perfluorinated gases, preferably from sulphur hexafluoride, perfluoropropane, perfluorobutanes, perfluoropentanes and perflurohexanes.

6. (once amended) [A]The method according to [any of claims 1 to 5]claim 1 wherein said gas is perfluorobutane and said surfactant is phosphatidylserine.

7. (once amended) [A]The method according to [any of claims 1 to 6]claim 1 wherein the microbubbles are removed before or after culturing, said removal is effected by bursting with a technique selected from ultrasonication, pH change or transient application of overpressure or underpressure.

10. (once amended) Use of microbubble-bound cells according to claim 8[or claim 9] for the investigation of diseases involving said receptors.

Claims (clean version encompassing amendments)

What is claimed is:

1. A method for the identification and investigation of a receptor in target tissue for which a selected vector has affinity, said method comprising:

i) creating retroviral particles containing a library of mRNA from the target tissue;

ii) transfecting a non-adherent cell line which does not bind with the selected vector by infecting the cells with said retroviral particles;

iii) adding to the transfected cell line a suspension of encapsulated gas microbubbles to which the selected vector is coupled and allowing the microbubbles and cells coupled thereto to float to the surface of the suspension;

iv) isolating the microbubble-bound cells at the surface;

and either

v-a) lysing the isolated cells, amplifying the receptor-encoding cDNA therefrom and sequencing said cDNA; and optionally

v-b) comparing the thus-obtained sequence data with gene bank sequence data;

or

vi–a) culturing the isolated cells; and

vi-b) investigating affinities of vectors to the isolated cells.

2. (once amended) The method according to claim 1 wherein said vector is selected from peptides, proteins, antibodies, nucleotides, hormones, growth factors, cytokines, carbohydrates, lipids, therapeutic agents and drugs acting through receptor-mediated cell entry.

3. (once amended) The method according to claim 1 wherein the encapsulated microbubbles of step iii) are selected from microbubbles of gas stabilised by a coalescence-resistant surface membrane, a filmogenic protein, a polymer material, a lipid, a non-polymeric and non-polymerisable wall-forming material and a surfactant.

4. (once amended) The method according to claim 3 wherein said surfactant is selected from one or more phospholipids and one or more lipopeptides.

5. (once amended) The method according to claim 1 wherein said gas is a biocompatible gas or gas mixture selected from perfluorinated gases, preferably from sulphur hexafluoride, perfluoropropane, perfluorobutanes, perfluoropentanes and perflurohexanes.

6. (once amended) The method according to claim 1 wherein said gas is perfluorobutane and said surfactant is phosphatidylserine.

7. (once amended) The method according to claim 1 wherein the microbubbles are removed before or after culturing, said removal is effected by bursting with a technique selected from ultrasonication, pH change or transient application of overpressure or underpressure.

8. Microbubble-bound transfected cells producible by method steps i) to iv) of claim 1.

9. Microbubble-bound transfected cells according to claim 8 wherein the microbubbles are of similar size to the transfected cells, preferably the microbubbles have diameters of 1 to 10 um, more preferably 3 to 5 um.

10. (once amended) Use of microbubble-bound cells according to claim 8 for the investigation of diseases involving said receptors.